



**Nanotechnology in Food and Consumer Products:
Promises, Possibilities, and Potential
Environmental and Health Implications?
A Whirlwind Tour**

WEHA Conference, April 28, 2009

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Overview of Today's Presentation

•What is nanotechnology?

Food, food safety, and agriculture applications

Potential benefits/Potential risks

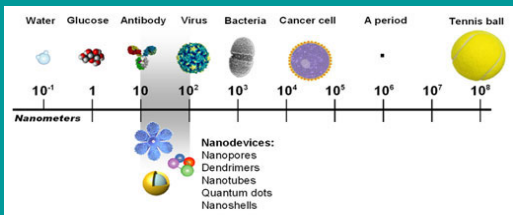
Case studies of specific nanomaterials

Data gaps, questions for future research

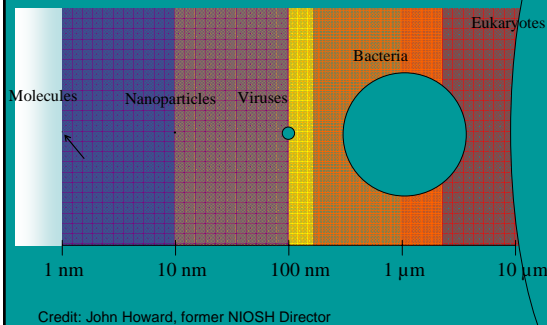
Conclusions & Questions

What is Nanotechnology?

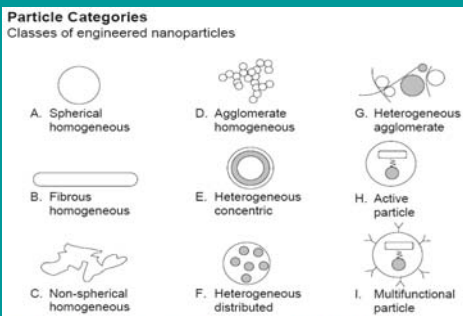
Nanotechnologies are the manipulation, precision placement, measurement, modeling, or manufacture of matter of 100 nanometers or less (U.S. NNI)



Size Comparisons

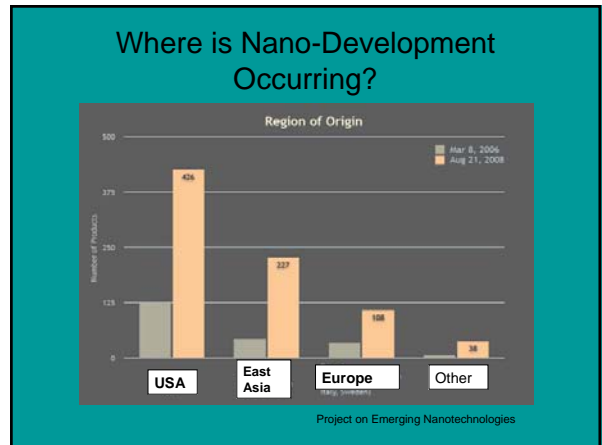
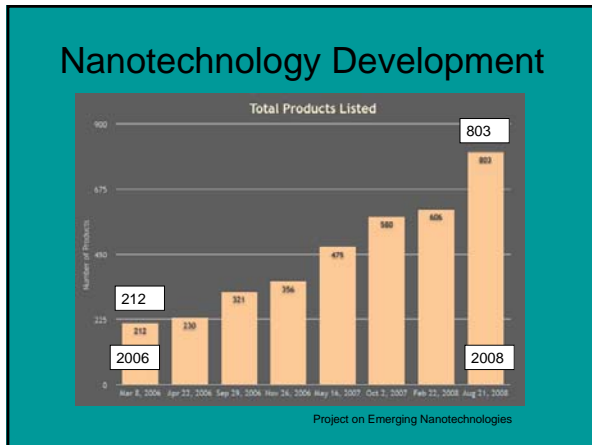
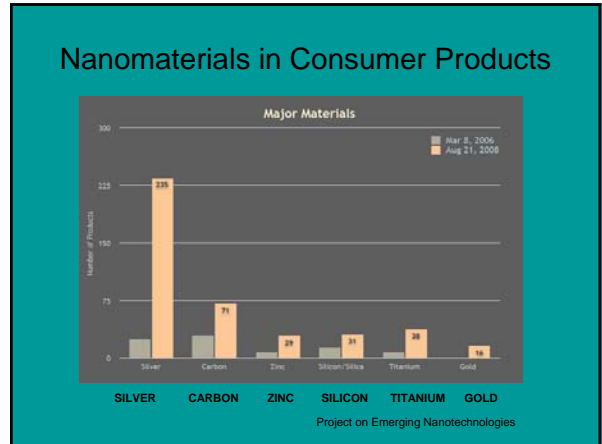
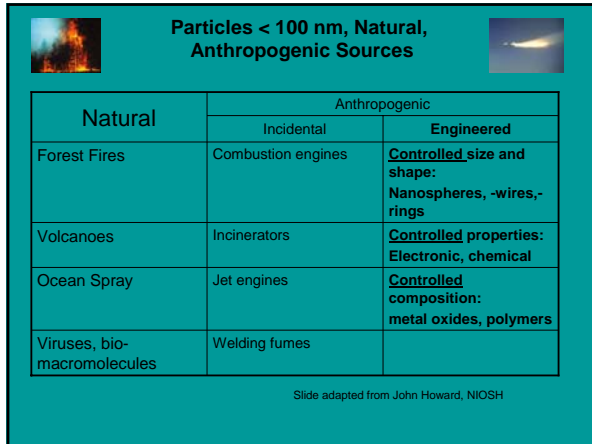


Different Shapes of Nanomaterials

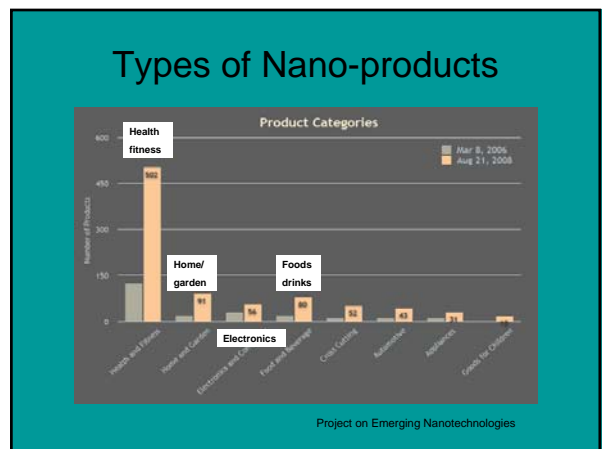


Nanotechnology is frequently referred to as "The Next Industrial Revolution." Why?

- **Useful properties at nanoscale:**
 - High surface-to-volume ratio
 - High conductivity, reactivity, strength & durability
 - Some nanomaterials (e.g., carbon nanotubes) 100s of times stronger than steel
- Nearly any material on periodic table can be nano-sized
- **But, nanomaterials (NMs) are not really new!**
 - NMs have been engineered for decades and have been used in computers for years
 - Nanomaterials are produced naturally & incidentally through a variety of human activities (e.g., combustion)



By 2014, products that incorporate nanotech will be 15% of global manufacturing, estimated total \$2.6 trillion (Lux Research)



Nano-products already on market



- Automotive, electronic
- Pharmaceuticals
- Many cosmetics, sunscreens
- Antibiotic coatings
- Food & food packaging
- Sporting goods
- "Electro textiles" or "Wired Wear"
- RFID chips
- "Smart dust"



Smith & Nephew Acticoat 7 antimicrobial wound dressing



Eddie Bauer Ruston Fit Nano-Care khakis



Wilson Double Core tennis balls

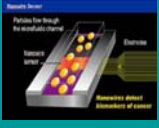
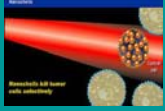
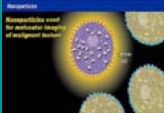


Kodak EasyShare LS633 camera

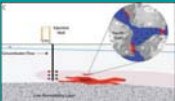
List of products on market: nanotechproject.org
How nanomaterials help these products work: nanoforum.org


Many beneficial applications beyond consumer products (no time to discuss today)

- Nanomedicine & health
 - more effective pharmaceuticals, antimicrobials
 - early detection/molecular imaging
 - improved medical devices
 - More...
- Improved industrial materials in all areas
 - lighter, stronger, more efficient
- Environmental
- Food, food safety, agriculture

Images from John Howard





- Applications that address existing environmental problems or prevent future problems:

Remediation & Pollution Control
Treatment
Pollution Detection & Monitoring
"Green" Nanotechnology

Nano for Food & Food Safety

- "Nanofood" market will grow to \$20.4 billion by 2010-2015
- Several hundred companies doing nanotech food research; expected to be several thousand by 2010
- 150-500 nano-based food and food-related products on the market worldwide
- See more news and reports here: http://www.nanocso.net/nanoproducts_food






High Hopes for Food Nanotechnology...

Recent Headline:
"Can Food Nanotechnology Make Junk Food Healthy?"




http://www.nanowork.com/news/newsid=9277.php

"Why can't human beings imitate nature's methodology? Instead of harvesting grain and cattle for carbohydrates and protein, Nanomachines could assemble the desired steak or flour from carbon, hydrogen, and oxygen atoms present in the air as water and carbon dioxide. Nanobots present in foods could circulate through the blood system, cleaning out fat deposits and killing pathogens."

Dr. Marvin Rudolph,
Director of DuPont Food Industry Solutions

Food and food packaging applications*



- **Food processing/ingredients:**
 - Nanoencapsulated oils and nutrients that do not affect flavor, color, clarity or texture of food
 - Nanoparticles and other nanostructures as gelation and viscosifying agents
 - Nanotechnology-based delivery systems for more potent, dispersible, bioavailable nutrient additives
 - Nano-sized versions of additives and nutrients that have already been used for a long time (e.g., titanium dioxide, iron oxide, zinc oxide)

* Some in development, some on the market



Example of product on the market: Nu-Mega

"Omega-3 DHA is an essential fatty acid, which cannot be manufactured in our body and must be obtained daily through our diets. Nu-Mega Ingredients is a world leader in the supply of Omega-3 DHA as an ingredient to the food industry, through our range of refined fish oils (tuna) and Driphorm® HiDHA® microencapsulated tuna oil.

Nu-Mega uses a patented microencapsulation technology that converts the HiDHA® tuna oil into a stable dry powder form (Driphorm®). This protects the tuna oil against oxidation and provides a form of taste barrier, such that manufacturers can increase the levels of Omega-3 DHA in a broad range of everyday foods, with minimal flavour impact and often without any alterations to product formulations."

Food and drinks that can change color "on demand"?*

"Are you ready for your Nanotechnology Engineered Wine?"
(Nanowerk News, Feb. 2007):

"Are you ready for your programmable wine - maybe a pico-pint or a nano-nebbiolo? Or want to take the red out of your red wine? Welcome to the world of nanofoods...Its mostly based on nano-encapsulation technology that will make nanotechnology engineered foods a reality. Researchers at US food giant Kraft have developed a colorless, tasteless liquid in the lab that consumers will design after you've bought it. You'll decide what color and flavor you'd like the drink to be, and what nutrients it will have in it, once you get home. You'll zap the product with a correctly-tuned microwave transmitter. This will activate nano-capsules - each one about 2,000 times smaller than the width of a hair - containing the necessary chemicals for your choice of drink: green-hued, blackcurrant-flavoured with a touch of caffeine and omega-3 oil, say."



* Not on market yet, but...

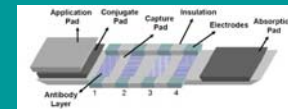
Nano-based food preservatives and antimicrobials

- Nanoparticles that remove or kill pathogens in food
- Refrigerators, baby bottles, food storage containers with nanosilver antimicrobials
- Surfaces designed to be permanently anti-microbial using nanotechnologies
- Nanoencapsulated preservatives and antimicrobials that are more potent and protected from degradation



Strawberries in a conventional food container (upper row) and nano-silver container (lower row). (Test series and pictures: The Innovation Society Ltd.) Taken from Nanowerks, Feb 16, 2009

Nanotechnology-based biosensors



- Mechanical, electrical and optical pathogen biosensors that rely on novel nanomaterials and biological materials (DNA, proteins, enzymes)
- Microarrays and 'labs-on-a-chip' that are portable, energy efficient, and can analyse several pathogens and parameters at once
- Biosensors that can detect chemical contaminants (pesticides and heavy metals)

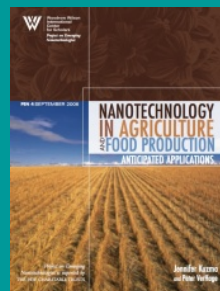


Nanotechnology and food packaging



- Films and packaging with better barrier properties, as well as lighter, stronger, and more heat resistant
- Films and packaging that can detect pathogens in foods and beverages by incorporating nanomaterials and/or biological materials
 - E.g., "Milk Cartons That Glow When the Milk Turns Sour?"
 - <http://www.bi-me.com/main.php?id=18292&t=1&c=33&cg=4>
- Encapsulation and delivery systems on packaging that release antimicrobials and other additives
- Packaging that incorporates RFID chips for tracking, detection of temp, moisture, etc
- "Intelligent" or "Smart" packaging systems for networked food and food product tracking

Nanotechnologies in Agriculture



- Nano-pesticides
- Nano-gene manipulation/"Atomically Modified Organisms" (AMOs)
- Synthetic biological materials for antibiotics, pesticides
- Facilitating germination with nanoparticles (e.g., iron)
- Nano soil binders to prevent erosion
- Soil cleanup using nanoparticles
- Biochips for DNA sequencing, disease detection
- Microfluidics for livestock breeding (sorting sperm & eggs)
- New pharmaceuticals and pharmaceutical delivery mechanisms
- "Smart" or "Little Brother" sensor systems

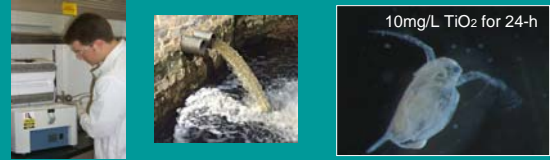
Potential Benefits of Nanotechnologies in Food & Agriculture?

Food:

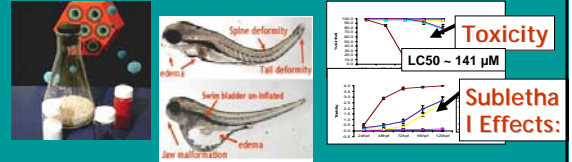
- Improved preservation of foods via better packaging and antimicrobials
- Improved aesthetic qualities of food/more consumer choices
- Production, processing, and shipment of food products could be safer and more secure (via better preservation, detection, and communication systems).

Agriculture:

- Possibly reduced use of pesticides (nano-pesticides are more targeted)
- Biosynthesis of new materials (pesticides, proteins, DNA) for disease treatment, pesticides, etc.
- "Smart systems" could increase efficiency & security of food systems and farms and reduce pesticide/fertilizer use.
- Protection of environment through reduction & conversion of agricultural materials into valuable products (vegetable oils, bio-based fuels).



But...as with all technologies, there may be risks...



Scientists, governments, insurance agencies, NGOs worldwide are raising concerns about potential risks related to emerging nanotechnologies:

- 2004 Royal Society/Royal Academy of Engineering Report
- 2004 Swiss Re Report/2005 Allianz Report
- Numerous government, NGO, and other reports since then...see: <http://www.nanoceo.net/nanoresources>



Why all the concern about nanotechnology?

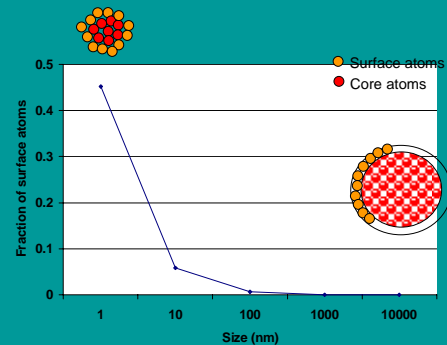
The same properties that make engineered nanomaterials so useful could make them more toxic than larger materials:



Critical issue--high surface-to-volume ratio that gives nanomaterials exciting properties, reactivity--also makes them likely to be more biologically reactive:

- 30 nm particle--5% of atoms on surface
- 10 nm particle--20% of atoms on surface
- 3 nm particle--50% of atoms on surface

Particles under 100 nanometers have much more surface area (relative to volume) than bigger particles!!



Adapted from John Howard

Many nanomaterials are strong oxidizers, can cause “oxidative stress” in cells...



What is oxidative stress?

- Natural process--causes apples to turn brown, butter to get rancid, aging of tissues
- Maintaining healthy cells requires a delicate balance between oxidizers and antioxidants: when there are too many oxidizers, oxidative stress results
- Oxidizing substances produce “free radicals” in cells, which have unpaired electrons and go hunting for “mates” to pair with these electrons
- Sometimes the nearest available molecules that can offer the free radical a mate are lipids, proteins, and DNA

Ongoing oxidative stress can lead to:

- Damage to lipids proteins, carbohydrates, and nucleic acids,
- Inflammation, cell death and eventually, disease.
- Associated with neurodegenerative disorders (Parkinson’s)

Existing knowledge about particle inhalation toxicology:

- Fine and ultrafine particles are associated with health effects in numerous inhalation toxicological studies
- Smaller particles are more reactive, deposit more deeply in lung tissue, cause oxidative stress.
- Because they are so reactive, smaller particles can absorb other substances and carry them into the lungs.
- Longer fibrous particles (e.g., asbestos) are not removed by bodily defenses (macrophages), stay in lungs longer and cause more damage
- All of the above factors can cause inflammation of lung tissue, leading to fibrosis, respiratory diseases, dysfunctional immune responses, and/or lung tumors.

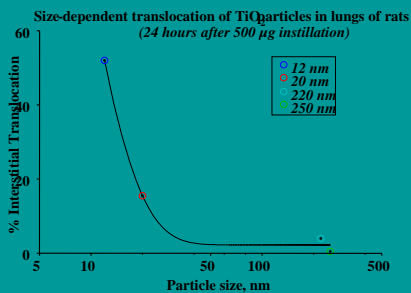
Epidemiological evidence: Effects of fine & ultrafine particulates in air pollution:

- A large and growing body of epidemiological research associates particulates in air pollution with respiratory and cardiovascular disease and mortality.
- Estimated that per 10 ug/m³ increase in PM_{2.5} in ambient air, overall mortality increases .9% and deaths from other respiratory diseases increase from 1.1 to 2.7%.

Studies to date suggest that nanoparticles (incidental and/or engineered) may affect more than lungs:

- Nano-sized particles can transport through barriers in body more readily than larger materials
- Can migrate into bloodstream and possibly contribute to cardiovascular problems (blood coagulation, atherosclerosis, heart attacks)
- Can translocate and build up in organs (liver, spleen, kidneys)
- Can be transported via axial nerve endings to olfactory bulb in brain (potential neurological effects?)
- Also, many engineered nanomaterials made of materials already known to be toxic (cadmium, lead, silver, etc) and/or known to be strong antimicrobials (silver)

Translocation: Titanium Dioxide



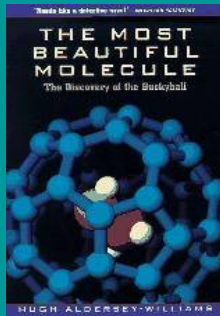
Translocation is a function of particle size (G. Oberdorster, EHP, 1992, 97, 193)

Slide adapted from John Howard, NIOSH

Are nanomaterials in consumer products of environmental health & safety concern?

Some examples (a whirlwind tour)...

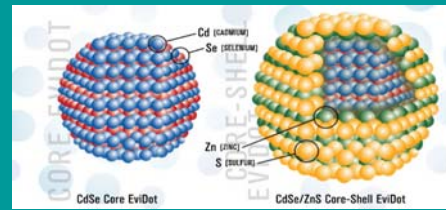
Buckminsterfullerenes or Fullerenes (“Buckyballs”)



- Used for catalysts, polymers, pharmaceuticals, cosmetics, sporting goods
- Can be strong anti-oxidants and oxidants, depending on conditions
- Considered for use in anti-AIDS drugs, antibiotics, antioxidants

Toxicological studies show:

- Tend to be strong oxidants in light
- Highly lipophilic—attracted to cell membranes
- Cause lipid peroxidation (a type of oxidative stress) in cell membranes
- Cause cell membrane “leakiness”
- Recent study—damage in fish brains?



• Quantum dots

- Crystalline, semi-conducting nanoparticles
- Used in electronics, biomedical tracking, paints, surveillance inks, surveillance dusts (smart dust or quantum dust)
- Cores usually made of cadmium or lead—both known toxins
- Early studies show that coatings on quantum dots can wear off, releasing cadmium and lead into cells/organisms (several zebra fish studies)



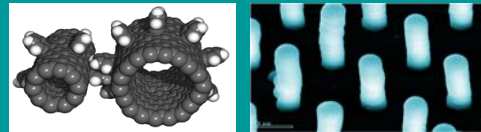
Titanium Dioxide

- Used in larger form as a whitening pigment for a long time
- Nano-sized titanium dioxide increasingly used in sunscreens, cosmetics, toothpaste, pharmaceuticals because it is transparent.
- Some animal studies associate titanium dioxide with cell damage, inflammations, fibrosis, DNA damage
- Can penetrate skin—will it cause damage when used in sunscreens, other cosmetics?



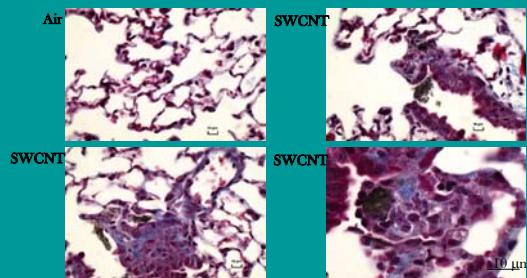
Carbon Nanotubes

- Like tube-shaped fullerenes; rolled up sheets of graphite
- Fibers—very high length-to-width or aspect ratio (like asbestos)
- Very light and extremely strong
- Used (or in development) for electronics, sporting goods, pharmaceuticals, construction materials, more...
- **Toxicological Studies:**
- In vitro studies show cellular changes, cytotoxicity, genetic effects
- Several animal studies show lung effects comparable to carbon black, silica, asbestos (?):
 - oxidative stress, inflammation, granulomas, fibrosis



Recent Study: Carbon Nanotube Toxicity to Respiratory Tract

Whole body inhalation exposure to SWCNT elicited acute inflammation combined with early progressive fibrosis and granulomas in mice.



A.A. Shvedova et al, *Am. J. Physiol. Lung Cell. Mol. Physiol.*, 2008, from John Howard, NIOSH

Another recent study on carbon nanotubes

- Direct exposure of the mesothelial lining of the body cavity of mice by intraperitoneal injection (50 µg dose)
- Acute (24h and 7 days) response
- Long (> 20 µm) straight MWCNT produced inflammatory response and formation of granulomas similar to asbestos fibers



Slide adapted from John Howard, NIOSH

Nanomaterials used in foods

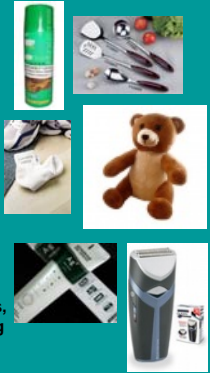
- Few available studies. Very little known about specific nanomaterials being used in foods/food packaging.
- Foods/drinks will be ingested (so we know there will be exposures)
- Nanomaterials for use in foods and "nanoceuticals" are often designed to be more soluble, more bioavailable, absorbed more readily, etc. This could result in overdoses of substances that are safe at lower levels. E.G.
 - One study showed that nano forms of chromium were absorbed by cells 3-5 times more efficiently than non-nano forms (Zha et al., 2008)
 - European Food Safety Authority (EFSA) concluded: Synthetic lycopene, a natural substance increasingly used in the nano-sized form to color foods and beverages "adds significantly to the overall intake of lycopene, and could result in intakes over the acceptable daily limit among children who consume lycopene-colored drinks regularly" (EFSA, 2008).

Nanosilver

Increasing use of nano-silver in numerous products, primarily as an antimicrobial:

- Nano socks and other nano textiles
- Kitchenware, food storage, other food items
- Samsung washing machines/refrigerators that emit silver ions into wash, fridge air
- Toys, personal care products
- Computer keyboards, office supplies
- Pet products

-Nano silver-titanium dioxide spray coating being used in trains, shopping malls, offices, and recreational facilities in Japan and Hong Kong to kill viruses, bacteria, other microorganisms



What is already known about silver?

- Silver in various bulk forms has been used for hundreds of years as an antimicrobial (also used in dental fillings, jewelry, photography, more...)
- Silver is generally thought to be safe for mammals, except at very high doses (e.g., argyria, argyrosis among silver workers)
- However, to date mostly case studies (no epidemiological studies)
- Silver ion is one of the most toxic heavy metals, 2nd most toxic after mercury. It is very toxic to non-mammalian species and of particular concern in aquatic environments.
- **Biological/cellular effects of silver ions:**
 - Bind to sulfhydryl groups, proteins, DNA, RNA, causing damage
 - Bind to several other important cellular molecules (glutathione)
 - Bind to membranes, causing damage and cellular leakage
 - Generate reactive oxygen species (oxidative stress)
 - Interact with zinc and calcium, may affect copper transport

Questions about nano-silver toxicity

- Will nanoparticulate forms of silver be more potent in releasing silver ions because of their high surface area?
- Will silver nanoparticles enter cells in ways that larger forms of silver cannot and continue to release silver ions?
- Will they carry other toxins into cells (Trojan Horse)?
- Will the increasing uses of nanosilver exacerbate antibacterial resistance problems in the gut (and environment)?

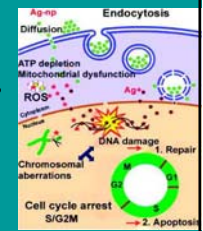


Diagram from AshaRani et al. 2009.

Recent in vitro and in vivo lab studies:

- Silver nanoparticles used in food storage interfere with DNA replication in cell culture (Yang et al, 2009)
- Genotoxicity, cytotoxicity of silver nanoparticles in human cells (AshaRani et al 2009)
- Several studies showing harm to zebrafish & other aquatic organisms (e.g., Griffith, 2008)

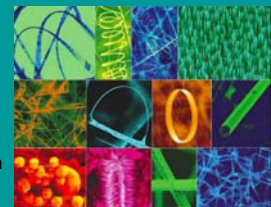
Overall Risk Assessment for Nanomaterials?

Risk characterization = HAZARD X EXPOSURE

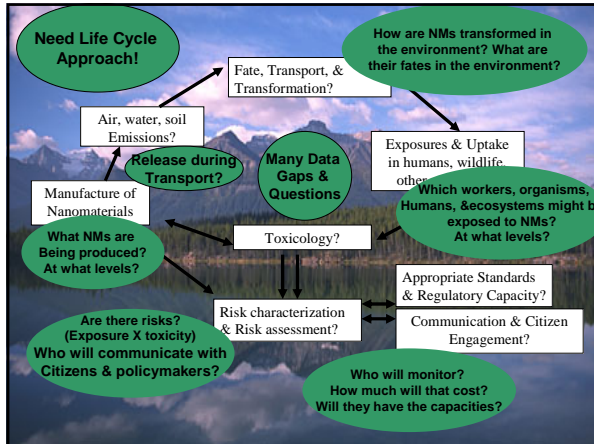
- Toxicological studies address **HAZARD** part of equation
- **At this point, there's little EXPOSURE data**
- What people and which ecosystems are likely to be exposed to nanomaterials, in what forms and at what levels (doses)?
 - ↓ ↓
- To know this, we need to know NM production levels, where NMs are produced and released, **fate/transport in the environment, and will they biodegrade/bioaccumulate**
- **Need to be able to monitor and characterize...**

Challenges characterizing & monitoring nanomaterials

- **Many parameters can affect their toxicities:**
 - Size
 - Shape/morphology
 - Surface area
 - Chemical composition
 - Surface functionalization
 - Chemical composition



- **MASS may not be most critical parameter (even though current standards mass-based)!**
- **Need to characterize nanomaterials very well in toxicological studies (more than just mass)**




Beginning of life cycle: Workplace exposures & effects?



- Nanomaterials are being created and handled in thousands of research labs & workplaces around the world.
- Many concerns & questions about ingestion, inhalation, dermal and other exposures to these materials
- Very few studies have monitored levels of nanomaterials in research labs and/or industrial workplaces
- Unfortunately, not enough time to go into this important topic here!

Videos with experts summarizing key nano EHS issues:
<http://mediasite.cae.wisc.edu/Mediasite/Catalog/Front.aspx?cid=40ab4565-ad49-43f8-8721-d84a015f51ee>

NIOSH Resources: Nanotechnology Topic Page



www.cdc.gov/niosh/topics/nanotech/

Environmental releases? Need to know if uses of nanomaterials are dispersive or not.


Inherently Dispersive (Free)



Not inherently Dispersive (Fixed)



Are nanomaterials emitted into the environment from production and/or consumer products?



- Modeling studies**
 - Model based on current production and use estimated that nano-TiO₂ particles likely to be found in significant concentrations in natural surface waters, at levels that could pose risks to aquatic life (Mueller & Nowack, 2008)
 - Mueller & Nowack estimated worldwide production of nanosilver as 500 tons and Blaser et al estimated that 50 tons/year of the silver emitted to water in Europe would come from nanosilver-containing biocidal plastics and textiles
- Actual releases from painted exteriors:**
 - Kaegi et al (2008) found that nano-TiO₂ particles between 20 and 300 nm were released from exterior paints and ended up in surface waters
- Nanosilver release from consumer products**
 - Benn & Westerhoff (2008) found significant levels of nanosilver released from socks with nanosilver currently on the market

UW State Lab of Hygiene/WI DNR project*

- How much silver (by mass) is in or released from consumer products claiming to have nanosilver in them?**
 - Nanosilver socks: 1.62-7.09 mg/Kg (ppm) silver in socks
 - Water from silver-ion generating washing machine—94.7 ug/L (ppb) silver
 - Levels of total silver in surface waters of the Midwest are typically less than 0.005 micrograms per liter (ppb)
 - Levels in food storage plastic bags (inside + outside)—24-27 ug of silver per BAG
 - Levels in leachate from bags**-- 1.32-1.65 ug of silver per BAG
 - About 1000 times typical levels in uncontaminated/well water.
- What can we conclude from this?**
 - Silver is released from these products at levels much higher than background

Numerous questions still need to be addressed:

- Is this silver in nanoparticulate form?
- Is more/less silver released in different conditions?
- Many more questions

* ICP-OES and ICP-MS analyses done by Martin Shafer, Dick Kittel, & DeWayne Kenney-Parker at the Wisconsin State Lab of Hygiene
 ** Bags were leached with acetic acid w/pH 4 to mimic fruit juice

Environmental Fate/Transport & Effects on Organisms?



- Will *NANO* forms of materials create new/exacerbated toxicities because of their high surface areas and other unique properties?
 - Will nanomaterials (NMs) be released at levels that will cause harm?
 - Will NMs aggregate, agglomerate, be soluble, etc. in various environments?
 - How will NMs interact with natural materials, environmental contaminants?
 - How will NMs be handled/treated in our water and sewage treatment systems?
 - Will NMs biodegrade, bioaccumulate in environment? Will they transform?
 - Will they be taken up by organisms? What effects might they have on them?
- Ultimately, need to address these questions (and more) to understand potential environmental and public health effects in the long-term

A few examples of other environmental studies to date:

Yang and Watts (2005): Examined phytotoxicity of aluminum oxide nanoparticles



Particles	Alumina and Silica nanoparticles
Organism	5 different plant species
Endpoint	Root elongation
Result	Alumina: Inhibition of root elongation

From Martye Griffin, Dept of Natural Resources

Effects on Aquatic Vertebrates:

Oberdorster (2004): Lipid oxidation in juvenile largemouth bass brains when exposed to THF-C60 (fullerene)



Oberdorster et al. (2005): 100% Fathead minnow mortality at 1 ppm THF-C60 (18h)



Oberdorster et al. (2006): 0% Fathead minnow mortality at 0.5 ppm water-C60 (96h)



Zhu et al. (2006): 0% Fathead minnow mortality 1 ppm water-C60 (96h)

From Martye Griffin, Dept of Natural Resources

Recent studies in *Environmental Pollution*

- Wang & Zing (2009): Metal oxide nanoparticles are toxic to nematodes (*C. elegans*), especially to reproductive capacities.
- Sun et al (2009): Accumulation of arsenic increased 44% in carp in presence of nano titanium dioxide
- Klaper et al (2009): Fullerene nanoparticles produce oxidative stress responses in *Daphnia*, but functionalization of the fullerenes can reduce toxicity.

Could engineered nanomaterials have broader public health effects?

- Extensive evidence from past toxicological & epidemiological studies shows that incidentally-produced nanoparticles can cause public health harm in workplaces and the environment.
- Growing number of lab-based studies suggests that purposely engineered nanomaterials may have some similar effects
- Engineered nanomaterials will definitely be widespread in workplaces, households, and the environment
- But, little monitoring or exposure data (environmental, workplace, or consumer exposure) on purposely engineered nanomaterials
- Environment effects and bioaccumulation/biomagnification could have subtle, long-term human effects (difficult to predict or detect).
- In other words, there are some "red flags," but we don't know!!

Summary

- Nanotechnologies promise many benefits in nearly every area, including environment and health
- At the same time, a growing number of studies suggest that there could be potential environmental and public health risks related to their production & use
- Life cycle approach is essential
- Important data gaps!
- Standards, regulations, policies may be inadequate for nanotechnology (see Powell et al., 2008)
- Limited funding to address research, policy, and communication data gaps in a timely manner.

Do our government, environmental and public health agencies have the capacities to be proactive, to prevent potential risks from emerging nanotechnologies?



Intergovernmental Nanotechnology Working Group

Building capacities among scientists, government agencies, citizens, and policymakers to address these risks proactively.

For Further Information:

- Nanotechnology Citizen Engagement Organization (NanoCEO): <http://www.nanoceo.net/>
- Project on Emerging Nanotechnologies: <http://www.nanotechproject.org/>
- International Council on Nanotechnology's Nano EHS Virtual Journal: <http://icon.rice.edu/virtualjournal.cfm>
- National Institute for Occupational Safety & Health (NIOSH): www.cdc.gov/niosh/topics/nanotech/
- SAFENANO (UK): <http://www.safenano.org/>

Questions?



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